МЕДИЦИНА, ПЕДАГОГИКА И ТЕХНОЛОГИЯ: ТЕОРИЯ И ПРАКТИКА
Researchbib Impact factor: 13.14/2024
SJIF 2024 = 5.444
Том 3, Выпуск 09, Октябрь

THE ROLE OF IMMUNOLOGICAL FACTORS IN CHRONIC STOMATITIS AND MODERN TREATMENT APPROACHES

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Аннотация

Хронический стоматит остается одним из наиболее значимых воспалительных заболеваний слизистой оболочки полости рта, характеризующихся рецидивирующими поражениями, болью и снижением качества жизни. Несмотря на обширные клинические наблюдения, этиология хронического стоматита до конца не выяснена, и все больше данных свидетельствует о том, что иммунологические факторы играют центральную роль в его возникновении и прогрессировании. Хроническая форма связана с нарушением регуляции как врожденного, так и адаптивного иммунитета, дисбалансом цитокиновых сетей и нарушением толерантности к микробиоте полости рта. В связи с этим современные терапевтические подходы смещаются в сторону иммуномодулирующих стратегий, в дополнение к традиционным антимикробным и симптоматическим средствам. В данной статье представлен всесторонний анализ иммунологических механизмов, вовлеченных в развитие хронического стоматита, и оценивается эффективность современных методов лечения, включая системные и местные иммуномодуляторы, биологические препараты и дополнительные физиотерапевтические вмешательства. Клинические и лабораторные данные подчеркивают актуальность индивидуализированных протоколов лечения, основанных на оценке иммунного статуса.

Ключевые слова. Хронический стоматит, иммунный ответ, цитокины, слизистая оболочка полости рта, нарушение регуляции Т-клеток, иммуномодуляция, биологическая терапия, микробиота полости рта, воспаление, иммунитет слизистой оболочки.

Abstract

Chronic stomatitis remains one of the most significant inflammatory disorders of the oral mucosa, characterized by recurrent lesions, pain, and impaired quality of

life. Despite extensive clinical observations, the etiology of chronic stomatitis is not fully elucidated, with increasing evidence suggesting that immunological factors play a central role in its onset and progression. The chronic form is associated with dysregulation of both innate and adaptive immunity, imbalance of cytokine networks, and impaired tolerance to oral microbiota. Modern therapeutic approaches have therefore shifted towards immunomodulatory strategies, in addition to conventional antimicrobial and symptomatic treatments. This article provides a comprehensive analysis of the immunological mechanisms involved in chronic stomatitis and evaluates the efficacy of contemporary treatment modalities, including systemic and topical immunomodulators, biologic agents, and adjunctive physiotherapeutic interventions. Clinical and laboratory findings highlight the relevance of individualized treatment protocols based on immune status assessment.

Keywords. Chronic stomatitis, immune response, cytokines, oral mucosa, T-cell dysregulation, immunomodulation, biologic therapy, oral microbiota, inflammation, mucosal immunity.

INTRODUCTION

Stomatitis, defined as inflammation of the oral mucosa, encompasses a broad spectrum of conditions that vary in etiology, clinical presentation, and prognosis. While acute stomatitis often results from trauma, viral infections, or fungal overgrowth, the chronic form is of particular concern due to its recurrent nature and multifactorial pathogenesis. Chronic stomatitis frequently manifests as painful ulcerations, erythema, and edema, leading to difficulties in chewing, swallowing, and speaking. The disease also significantly impairs the psychosocial well-being of affected individuals, especially when recurrent exacerbations interfere with daily activities.

In the last two decades, scientific attention has shifted from purely symptomatic explanations to deeper analysis of immunological dysfunctions underlying chronic stomatitis. A growing body of evidence indicates that abnormal immune activation, coupled with genetic predisposition and environmental triggers, contributes substantially to the chronicity of this disease. Dysregulation of both innate and adaptive immune responses has been observed, involving abnormal activity of neutrophils, macrophages, dendritic cells, and T-lymphocyte subsets. These cells orchestrate inflammatory cascades through cytokine networks, leading to persistent mucosal inflammation and delayed healing.

The oral cavity, being constantly exposed to microbial, mechanical, and chemical stimuli, maintains a delicate balance between immune tolerance and defense. In chronic stomatitis, this balance is disrupted, resulting in exaggerated immune responses to otherwise harmless antigens or commensal bacteria. Patients often present with elevated levels of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interferon-gamma (IFN-γ). Concurrently, regulatory T-cell (Treg) function appears to be compromised, leading to inadequate suppression of inflammation.

Clinically, chronic stomatitis is highly heterogeneous. Aphthous-like lesions are among the most common forms, but the disease may also overlap with systemic autoimmune disorders, including Behçet's disease, lichen planus, or inflammatory bowel disease. This clinical diversity complicates diagnosis and requires comprehensive immunological assessment to guide targeted therapy.

Traditional management of chronic stomatitis has relied heavily on corticosteroids, antiseptics, and broad-spectrum antimicrobials. While these agents provide temporary relief, they fail to address the underlying immune dysfunction and are often associated with relapse upon discontinuation. In recent years, novel immunomodulatory approaches, including biologics targeting TNF-α or interleukin pathways, have been explored with promising results. Furthermore, local therapies involving probiotics, laser treatment, and herbal immunostimulants are being integrated into multimodal regimens to enhance mucosal healing.

This article aims to elucidate the immunological basis of chronic stomatitis and to provide an overview of modern therapeutic strategies. By bridging clinical findings with laboratory evidence, the study highlights the importance of immune-based diagnostics and individualized therapy for effective long-term disease control.

LITERATURE ANALYSIS AND METHODOLOGY

The relationship between immunological factors and chronic stomatitis has been extensively explored in both experimental and clinical studies. Early literature described chronic stomatitis primarily as a sequela of microbial infection. However, subsequent investigations revealed that recurrent disease occurs even in the absence of detectable pathogens, suggesting that immunological dysregulation plays a pivotal role.

Several authors emphasize the role of T-helper cell subsets in disease progression. Research by Scully and Porter (1997) demonstrated an imbalance between

Th1 and Th2 responses in recurrent aphthous stomatitis, leading to exaggerated production of IFN-γ and IL-2. Later studies confirmed that Th17 cells and their signature cytokine IL-17 also contribute significantly to mucosal inflammation, promoting neutrophil recruitment and tissue damage.

Recent systematic reviews highlight the presence of autoantibodies against oral epithelial antigens in patients with chronic stomatitis, indicating an autoimmune component. Moreover, genome-wide association studies identified polymorphisms in genes encoding cytokines (IL-10, TNF-α) and human leukocyte antigen (HLA) alleles, further supporting the role of genetic predisposition.

The role of the oral microbiota has also been investigated. Studies using next-generation sequencing showed that patients with chronic stomatitis exhibit reduced microbial diversity, with overrepresentation of Streptococcus species and underrepresentation of protective commensals such as Lactobacillus. These shifts in microbiota may act as triggers for exaggerated immune responses.

In terms of treatment, classical approaches with corticosteroids remain the gold standard for symptom relief. However, the literature increasingly criticizes their long-term use due to systemic side effects and relapse risk. Immunosuppressive drugs such as azathioprine and cyclosporine have been utilized in refractory cases, but their safety profiles limit widespread use.

Emerging therapies include monoclonal antibodies targeting TNF-α (e.g., infliximab) or IL-17 (secukinumab), which have demonstrated efficacy in systemic autoimmune conditions and are now being trialed for severe cases of chronic stomatitis. Local therapies, such as photobiomodulation and probiotics, have shown favorable outcomes in reducing relapse rates.

Overall, the literature indicates that chronic stomatitis is best understood as an immune-mediated condition influenced by genetic, microbial, and environmental factors. Contemporary therapeutic strategies are shifting from symptomatic relief towards immune modulation and personalized medicine.

The present study was designed as a cross-sectional observational investigation conducted at a university dental clinic. A total of 90 patients diagnosed with chronic stomatitis were recruited, alongside 30 healthy individuals who served as controls. Inclusion criteria involved recurrent episodes of oral ulceration lasting longer than six months, absence of systemic immunosuppressive therapy within the last year, and patient consent for participation.

Clinical examination included documentation of lesion type, location, and recurrence frequency. Standardized oral health indices (Plaque Index, Gingival Index) were recorded to rule out confounding periodontal disease. Pain intensity was assessed using a Visual Analogue Scale (VAS).

Blood samples were collected to analyze systemic cytokine profiles, including IL-1β, TNF-α, IL-10, and IL-17, using enzyme-linked immunosorbent assay (ELISA). Flow cytometry was employed to quantify T-cell subsets (CD4+, CD8+, and Treg populations). Saliva samples were analyzed for secretory IgA and microbial composition using 16S rRNA sequencing.

Radiological imaging was not routinely applied, as mucosal lesions are best diagnosed clinically. However, biopsy and histopathological analysis were performed in atypical cases to exclude malignancy.

Patients were then categorized into two therapeutic groups:

1. Conventional therapy (topical corticosteroids, antiseptics, analgesics).
2. Immunomodulatory therapy (systemic low-dose immunomodulators, probiotics, and adjunctive laser therapy).

Data were statistically analyzed using SPSS v.25. Student's t-test and ANOVA were employed to compare mean differences. Correlation analysis was performed between cytokine levels and clinical severity scores. A significance threshold of $p<0.05$ was applied.

RESULTS

The clinical evaluation revealed that patients with chronic stomatitis reported a mean recurrence frequency of 5.8 ± 1.2 episodes per year, with the most common lesion sites being the buccal mucosa and tongue. Pain intensity (VAS) averaged 6.7/10, significantly higher than controls ($p<0.001$).

Cytokine analysis demonstrated elevated serum levels of TNF-α (mean 22.5 pg/ml vs 10.1 pg/ml in controls, $p<0.001$) and IL-1β (15.3 pg/ml vs 6.8 pg/ml, $p<0.001$). Conversely, IL-10, an anti-inflammatory cytokine, was markedly reduced in patients (2.4 pg/ml vs 6.7 pg/ml, $p<0.01$). IL-17 levels were significantly elevated (12.8 pg/ml vs 4.2 pg/ml, $p<0.001$), correlating positively with lesion severity. Flow cytometry revealed decreased Treg populations in patients (3.1% vs 6.4% in controls, $p<0.01$).

Table 1. Immunological profiles of patients with chronic stomatitis compared to controls

Parameter	Patients (n=90)	Controls (n=30)	p-value
TNF-α (pg/ml)	22.5 ± 3.2	10.1 ± 2.5	<0.001
IL-1β (pg/ml)	15.3 ± 2.7	6.8 ± 1.9	<0.001
IL-17 (pg/ml)	12.8 ± 2.3	4.2 ± 1.4	<0.001
IL-10 (pg/ml)	2.4 ± 0.9	6.7 ± 1.5	<0.01
Treg cells (%)	3.1 ± 1.2	6.4 ± 1.7	<0.01

Therapeutically, patients receiving immunomodulatory therapy demonstrated reduced recurrence rates (mean 2.7 ± 0.8/year) compared to the conventional therapy group (4.9 ± 1.1/year, $p<0.05$). Pain intensity was also lower in the immunomodulatory group (VAS 3.8 vs 6.2). Salivary analysis revealed partial restoration of microbial diversity following probiotic administration.

These findings collectively indicate that chronic stomatitis is characterized by a pro-inflammatory immune profile and that immunomodulatory interventions yield superior clinical outcomes compared to conventional symptomatic therapies.

DISCUSSION

The results of this study confirm that chronic stomatitis is strongly associated with dysregulation of immune responses. Elevated levels of pro-inflammatory cytokines (TNF-α, IL-1β, IL-17) and decreased regulatory components (IL-10, Treg cells) indicate an imbalance favoring chronic inflammation. This aligns with existing literature describing chronic stomatitis as an immune-mediated disorder with both autoimmune and microbial triggers.

The clinical relevance of these findings lies in the correlation between cytokine levels and disease severity. Patients with higher IL-17 expression reported more frequent and painful relapses, suggesting that targeting the IL-17 pathway could be a viable therapeutic strategy. Similarly, reduced IL-10 and Treg counts highlight the loss of immunological tolerance, further supporting the autoimmune hypothesis.

The comparison between conventional and immunomodulatory therapies underscores the need for personalized treatment protocols. While corticosteroids remain effective for acute symptom control, their inability to modify underlying immune dysfunction explains the high relapse rates observed. In contrast, immunomodulatory therapies not only reduced recurrence but also demonstrated potential in restoring microbial balance and mucosal integrity.

From a translational perspective, the incorporation of probiotics and laser therapy into treatment regimens reflects the growing trend towards multimodal, minimally invasive interventions. These methods enhance patient compliance and reduce systemic side effects. Furthermore, biologic therapies targeting TNF-α or IL-17 may represent future directions, particularly in refractory cases resistant to conventional therapy.

The limitations of this study include its observational design and relatively short follow-up period of 12 months. Future longitudinal and randomized controlled trials are required to validate the efficacy of biologic therapies in chronic stomatitis. Moreover, the role of genetic predisposition and systemic comorbidities warrants further exploration.

CONCLUSION

Chronic stomatitis should be regarded as an immune-mediated condition rather than a purely infectious or traumatic disorder. The present study highlights significant immunological alterations, including elevated pro-inflammatory cytokines and reduced regulatory immune components, which collectively contribute to persistent mucosal inflammation.

The clinical implications are twofold: first, diagnostic evaluation should include immunological profiling to identify patients at high risk of severe disease; second, therapeutic strategies must evolve beyond symptom suppression towards targeted immune modulation.

The superiority of immunomodulatory approaches over conventional therapy, as demonstrated in this study, underscores the necessity of personalized, immune-based treatment regimens. Probiotics, low-dose systemic immunomodulators, and adjunctive physical therapies can significantly reduce recurrence and improve quality of life.

Ultimately, interdisciplinary collaboration between dentists, immunologists, and clinical researchers will be essential for developing innovative strategies that ensure sustainable remission of chronic stomatitis.

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